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Acid-catalyzed regioselective sulfamination of γ-amino–alkenes and stereoselective rearrangement of pyrrolidines to piperidines

Lijun Li [a], Haining Wang [a], Deshun Huang [a], Yian Shi [a,b,*]

[a] Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

[b] Department of Chemistry, Colorado State University, Fort Collins, CO 80523, United States

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ABSTRACT

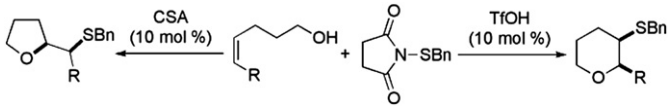
This paper describes efficient acid-catalyzed regioselective sulfamination of γ-amino–alkenes to form pyrrolidines and stereoselective rearrangement of pyrrolidines to piperidines. A possible reaction mechanism has been proposed.

1. Introduction

Pyrrolidines and piperidines are very important functional moieties that are present in various biologically active compounds.[1] Electrophilic cyclization of γ-amino–alkenes provides a straightforward approach to pyrrolidines and piperidines.[2–6] Our previous studies have shown that either tetrahydrofurans or tetrahydropyrans can be regioselectively formed from alkenols with sulfenamides depending upon acid catalysts used (Scheme 1).[7–9] Mechanistic studies indicate that tetrahydrofurans are kinetically favoured products and can stereoselectively rearrange to thermodynamically favoured tetrahydropyrans under acid conditions.[9] These observations prompted us to investigate whether similar transformations can be achieved with γ-amino–alkenes to form synthetically useful pyrrolidines and piperidines. Herein, we wish to report our efforts on this subject.

2. Results and discussion

The cyclizations of γ-amino–alkenes (**1a**–**e**) with different substituents on the nitrogen atom were examined with methyl benzenesulfenate (**2**) as the sulfur source[10,11] and CSA or TfOH as catalyst (Table 1, entries 1–5). In all the cases except for *N*-ethyloxycarbonyl γ-amino–alkene **1a**, pyrrolidines were formed in high yields (84–95%) and high regioselectivity. Considering the easy removal of the Ns group, various *N*-2-nitrobenzenesulfonyl γ-amino–alkenes (**1f**–**l**) were subsequently investigated with CSA, TfOH, and TsOH (Table 1, entries 6–12). In all the cases, 5-*exo*-products **3** were formed predominately in good yields (73–91%) (for X-ray structure of **3j**, see Supplementary data). For some *trans*-olefins, small amounts of 6-*endo* products were formed (Table 1, entries 9 and 11). In general, *trans*-γ-amino–alkenes give significantly higher 5-*exo* selectivity than *trans*-γ-hydroxy–alkenes.[9] The cyclization also proceeded diastereoselectively. *cis*-Olefins gave *threo*-products (Table 1, entries 1–8), and *trans*-olefins gave *erythro*-products (Table 1, entries 9–12). No other diastereoisomers were detected by ^{1}H NMR spectroscopic analysis of the crude products.



Scheme 1.

The rearrangement was examined with isolated pyrrolidine **3** and TfOH in CH_2Cl_2 at 25 °C. As shown in Table 2, piperidine **4** was formed as a major product except for entry 7. In some cases, piperidine **4** could be separated from the corresponding pyrrolidine

* Corresponding author. E-mail address: yian@lamar.colostate.edu (Y. Shi).

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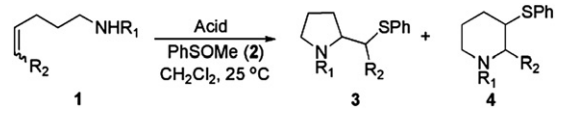
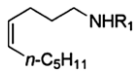
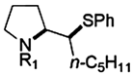
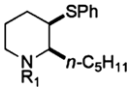
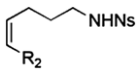
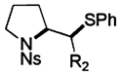
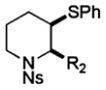
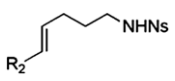
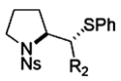
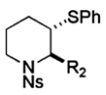
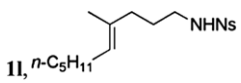
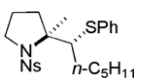
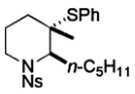
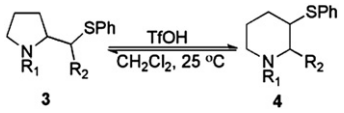
Table 1
Sulfamination of γ-amino–alkenes[a]

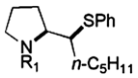
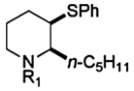
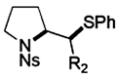
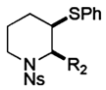
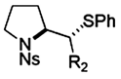
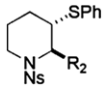


Entry	Substrates	Ratio **3**:**4**[e]	Yield (%) (**3**)[f]
			
1	**1a**, R_1=CO_2Et	Multiple products	
2	**1b**, R_1=Ts	>99:1	95
3	**1c**, R_1=Mts	>99:1	89
4	**1d**, R_1=4-Ns	>99:1	84
5[b]	**1e**, R_1=Ns	>99:1	93
			
6[b]	**1f**, R_2=H	>99:1	88
7[c]	**1g**, R_2=CH_3	>99:1	86
8[b]	**1h**, R_2=*t*-Bu	>99:1	73
			
9[c]	**1i**, R_2=*n*-C_5H_{11}	92:8	91
10[c]	**1j**, R_2=Cy	>99:1	87
11[c]	**1k**, R_2=*i*-Bu	93:7	77
12[d]			
	1l, *n*-C_5H_{11}		88

[a] Reactions were carried out with substrate **1** (0.50 mmol), PhSOMe (**2**) (0.60 mmol), and CSA (0.05 mmol) in CH_2Cl_2 (2.5 mL) at 25 °C for 1 h unless otherwise stated. Ts=*p*-toluenesulfonyl; Mts=2,4,6-trimethylbenzenesulfonyl; 4-Ns=4-nitrobenzenesulfonyl; Ns=2-nitrobenzenesulfonyl; CSA=10-camphorsulfonic acid; TsOH=*p*-toluenesulfonic acid; TfOH=trifluoromethanesulfonic acid.
[b] With TfOH (0.05 mmol) in CH_2Cl_2 (5.0 mL).
[c] With PhSOMe (**2**) (1.0 mmol) and TsOH·H_2O (0.10 mmol) in CH_2Cl_2 (5.0 mL) for 12 h.
[d] In CH_2Cl_2 (5.0 mL) for 12 h.
[e] The ratio was determined by ^{1}H NMR spectroscopic analysis of the crude product.
[f] Isolated yield of **3**.

Table 2
Rearrangement of pyrrolidines to piperidines[a]



Entry	Substrates (**3**)	Time (h)	Ratio **3**:**4**[d]	Yield (%)[e]
				
1	**3b**, R_1=Ts	12	32:68	99
2[b]	**3c**, R_1=Mts	48	12:88	80[f]
3	**3d**, R_1=4-Ns	12	29:71	99
4	**3e**, R_1=Ns	12	12:88[h]	86[f]
				
5[c]	**3f**, R_2=H	24	11:89	98
6	**3g**, R_2=CH_3	12	10:90	96
7	**3h**, R_2=*t*-Bu	48	95:5	-[g]
				
8	**3i**, R_2=*n*-C_5H_{11}	12	12:88	82[f]
9	**3j**, R_2=Cy	24	15:85	60[f]
10	**3k**, R_2=*i*-Bu	24	16:84	81[f]

[a] Reactions were carried out with substrate **3** (0.50 mmol), TfOH (0.05 mmol) in CH_2Cl_2 (2.5 mL) at 25 °C unless otherwise stated.
[b] With TfOH (0.10 mmol).
[c] With TfOH (0.50 mmol).
[d] The ratio was determined by ^{1}H NMR spectroscopic analysis of the crude product.
[e] Isolated yield of mixture **3** and **4** unless otherwise noted.
[f] Isolated yield of **4**.
[g] Trace amounts of **4 h** were detected by ^{1}H NMR spectroscopic analysis of the crude product.
[h] The ratio did not change after 72 h.

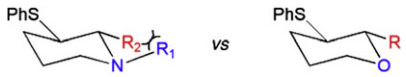
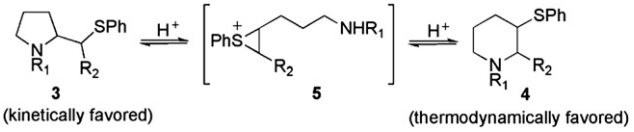


Fig. 1. The steric hindrance caused by the N-substituent in piperidine.



Scheme 2.

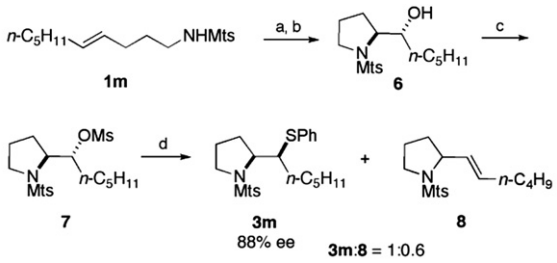
by column chromatography (Table 2, entries 2, 4, 8–10) (for X-ray structures of sulfone derivatives of **4e** and **4j** see Supplementary data). The ratio of piperidine to pyrrolidine was found to be generally lower than that of tetrahydropyran to tetrahydrofuran,[9] which is likely due to the steric hindrance caused by the *N*-substituent in piperidine as compared to the corresponding tetrahydropyran (an example is shown in Fig. 1).[12] When R_2=*t*-Bu, little piperidine was formed (Table 2, entry 7).

As in the case of the rearrangement of tetrahydrofuran to tetrahydropyran,[9,13] pyrrolidine **3** is the kinetically favoured product and can be stereoselectively rearranged to the thermodynamically favoured piperidine product **4** in the presence of acid catalyst TfOH, likely via thiiranium ion intermediate **5** (Scheme 2).

To probe the reaction mechanism, optically active compounds **3m** and **16** were prepared. The synthesis of pyrrolidine **3m** is outlined in Scheme 3. Asymmetric epoxidation[14] of **1m** followed by cyclization gave alcohol **6** in 61% yield over two steps. Compound **3m** was obtained from **6** by mesylation[15] and nucleophilic substitution with NaSPh.[16]

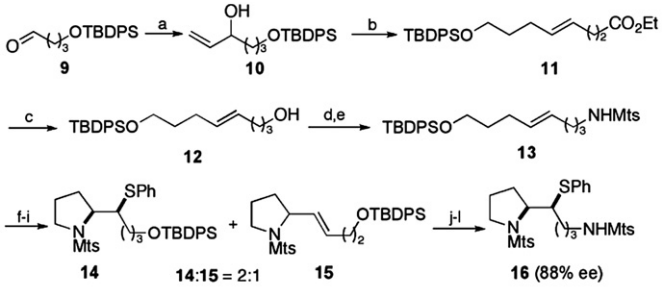
The preparation of pyrrolidine **16** is shown in Scheme 4. Compound **10**, prepared by the addition of vinylmagnesium bromide to aldehyde **9**,[17] was converted to ester **11** by Johnson–Claisen rearrangement.[18–20] Amino-alkene **13** was obtained from ester **11** by reduction with $LiAlH_4$, mesylation, and nucleophilic substitution.[15] Compound **13** was converted to pyrrolidine **14** in a manner similar to the reaction sequence from **1m** to **3m**. Compound **16** was synthesized from **14** by desilylation, mesylation, and nucleophilic substitution.

Treating enantiomerically enriched pyrrolidine **3m** with TfOH (1.0 equiv) in CH_2Cl_2 at 25 °C led to the formation of optically active piperidine product **4m** in 78% yield without erosion of ee, suggesting that the rearrangement proceeded via configurationally stable thiiranium ion **5m** (Scheme 5).[9,21,22] The involvement of



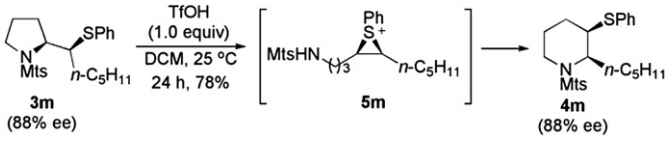
a) D-fructose-derived ketone catalyst, n-Bu_4NHSO_4, K_2CO_3/HOAc, DMM/CH_3CN, Na_2EDTA, Oxone, K_2CO_3, 0 °C. b) CSA, DCM, rt, 61% over two steps. c) MsCl, Et_3N, THF, 0 °C to rt. d) NaSPh, THF, reflux, 27% for **3m** from **6**.

Scheme 3.



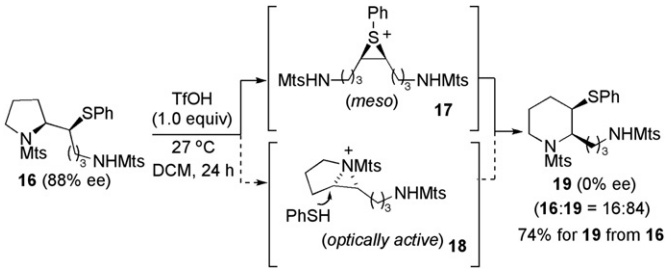
a) Vinylmagnesium bromide, THF, -40 °C to rt, 89%. b) Triethyl orthoacetate, propionic acid, 138 °C, 82%. c) $LiAlH_4$, 0 °C to rt, 92%. d) MsCl, Et_3N, THF, 0 °C to rt. e) $MtsNH_2$, KOH, DMF, 120 °C, 67% over two steps. f) D-fructose-derived ketone catalyst, n-Bu_4NHSO_4, K_2CO_3/HOAc, DMM/CH_3CN, Na_2EDTA, Oxone, K_2CO_3, 0 °C. g) CSA, DCM, rt. h) MsCl, Et_3N, THF, 0 °C to rt. i) NaSPh, THF, reflux, 35% over four steps. j) TBAF, THF, rt. k) MsCl, Et_3N, THF, 0 °C to rt. l) $MtsNH_2$, KOH, DMF, 120 °C, 64% over three steps.

Scheme 4.



Scheme 5.

a thiiranium ion intermediate during the rearrangement was further supported by the fact that racemic piperidine **19** was obtained when optically active pyrrolidine **16** was subjected to the reaction conditions. It is likely that the rearrangement proceeded via *meso* thiiranium ion intermediate **17** rather than optically active aziridinium ion intermediate **18** (Scheme 6).[9,23]



Scheme 6.

3. Conclusion

In summary, we have developed an efficient acid-catalyzed regioselective and diastereoselective sulfamination of γ-aminoalkenes to form pyrrolidines in high yields. The resulting pyrrolidines can be stereoselectively rearranged to piperidines via a thiiranium ion intermediate in the presence of strong acid TfOH. The current work provides a viable method to synthesize useful pyrrolidines and piperidines as well as better understanding of the thiiranium ion-based rearrangement.

4. Experimental section

4.1. General information and materials

All commercially available reagents were used without further purification. All dry solvents were freshly distilled under nitrogen from appropriate drying agents before use. Toluene, tetrahydrofuran, and ethyl ether were distilled from sodium–benzophenone. CH_2Cl_2 was distilled from CaH_2. $CHCl_3$ was distilled from P_2O_5. Column chromatography was performed on silica gel (200–300 mesh). ^1H NMR spectra were recorded on a 400 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FTIR spectrometer. High resolution mass spectra (HRMS) were obtained using EI-TOF or ESI-FTICR mass spectrometer. Melting points were uncorrected.

Compounds **1a**–**e**, **1g**, **1i**, and **1m** were prepared from commercially available alcohols by tosylation, azidation, reduction with $LiAlH_4$, and subsequent protection.[15,24] Compound **1f** was prepared by Mitsunobu reaction from the corresponding alcohol.[25] Compound **1h** was prepared by Wittig reaction[26] and Mitsunobu reaction.[25] Compounds **1j**–**l** were prepared by Johnson–Claisen rearrangement,[18] reduction, and Mitsunobu reaction.[25]

4.2. Representative procedure for acid-catalyzed sulfamination (Table 1, entry 2)

To a stirred solution of benzenesulfenate (**2**) (0.084 g, 0.60 mmol) and alkene **1b** (0.155 g, 0.50 mmol) in CH_2Cl_2 (2.5 mL) was added CSA (0.012 g, 0.05 mmol) at 25 °C. Upon stirring at 25 °C for 1 h, the reaction mixture was filtered through a plug of silica gel with CH_2Cl_2 as eluent, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=40:1) to give compound **3b** as white solid (0.199 g, 95%).

*4.2.1. threo-2-[1-(Phenylthio)hexyl]-1-tosylpyrrolidine (**3b**) (Table 1, entry 2).* White solid; mp 105–107 °C; IR (film) 1345, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J=7.2 Hz, 2H), 7.41–7.33 (m, 4H), 7.33–7.26 (m, 1H), 7.15 (d, J=8.0 Hz, 2H), 3.90 (dt, J=11.6, 3.2 Hz, 1H) 3.62–3.53 (m, 1H), 3.51–3.38 (m, 1H), 3.27–3.16 (m, 1H), 2.37 (s, 3H), 1.98–1.85 (m, 2H), 1.80–1.62 (m, 3H), 1.58–1.42 (m, 1H), 1.42–1.20 (m, 6H), 0.92 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 135.6, 133.6, 131.4, 129.7, 129.3, 127.8, 126.7, 62.2, 51.8, 51.2, 32.0, 27.8, 27.5, 26.8, 24.6, 22.8, 21.7, 14.3; Anal. Calcd for $C_{23}H_{31}NO_2S_2$: C, 66.15; H, 7.48; N, 3.35; found: C, 65.99; H, 7.55; N, 3.33.

*4.2.2. threo-1-(Mesitylsulfonyl)-2-[1-(phenylthio)hexyl]pyrrolidine (**3c**) (Table 1, entry 3).* Pale yellow oil; IR (film) 1604, 1467, 1314 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.13 (m, 5H), 6.88 (s, 2H), 4.15–4.07 (m, 1H), 3.69–3.58 (m, 1H), 3.23–3.14 (m, 1H), 2.91–2.82 (m, 1H), 2.49 (s, 6H), 2.29 (s, 3H), 2.19–2.08 (m, 1H), 2.07–1.94 (m, 1H), 1.85–1.75 (m, 2H), 1.67–1.52 (m, 2H), 1.33–1.11

(m, 5H), 1.07–0.92 (m, 1H), 0.88 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 140.3, 135.3, 133.4, 132.2, 131.6, 129.1, 126.9, 62.1, 52.5, 49.9, 32.0, 28.5, 27.8, 27.6, 25.4, 22.9, 22.8, 21.1, 14.2; Anal. Calcd for $C_{25}H_{35}NO_2S_2$: C, 67.37; H, 7.92; N, 3.14; found: C, 67.25; H, 7.85; N, 3.13.

*4.2.3. threo-1-(4-Nitrophenylsulfonyl)-2-[1-(phenylthio)hexyl]-pyrrolidine (**3d**) (Table 1, entry 4).* White solid; mp 139–141 °C; IR (film) 1522, 1159 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J*=8.8 Hz, 2H), 7.60–7.49 (m, 4H), 7.46–7.33 (m, 3H), 3.89 (dt, *J*=11.6, 3.2 Hz, 1H) 3.58–3.44 (m, 2H), 3.25–3.16 (m, 1H), 2.05–1.92 (m, 1H), 1.90–1.65 (m, 4H), 1.58–1.45 (m, 1H), 1.45–1.20 (m, 6H), 0.93 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 142.1, 135.2, 132.2, 129.4, 128.9, 127.3, 124.3, 62.5, 52.1, 51.4, 31.9, 27.7, 27.4, 26.8, 24.6, 22.8, 14.3; Anal. Calcd for $C_{22}H_{28}N_2O_4S_2$: C, 58.90; H, 6.29; N, 6.24; found: C, 58.74; H, 6.35; N, 6.15.

*4.2.4. threo-1-(2-Nitrophenylsulfonyl)-2-[1-(phenylthio)hexyl]-pyrrolidine (**3e**) (Table 1, entry 5).* White solid; mp 78–81 °C; IR (film) 1546, 1372, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.59 (m, 1H), 7.56–7.41 (m, 5H), 7.39–7.32 (m, 2H), 7.32–7.25 (m, 1H), 4.02–3.94 (m, 1H), 3.78–3.69 (m, 1H), 3.69–3.60 (m, 1H), 3.49–3.38 (m, 1H), 2.07–1.97 (m, 2H), 1.90–1.57 (m, 4H), 1.40–1.19 (m, 6H), 0.88 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 135.5, 133.6, 131.6, 131.3, 131.2, 129.3, 127.0, 124.1, 63.0, 52.2, 51.2, 31.9, 27.8, 27.6, 27.3, 25.0, 22.8, 14.3; Anal. Calcd for $C_{22}H_{28}N_2O_4S_2$: C, 58.90; H, 6.29; N, 6.24; found: C, 59.04; H, 6.46; N, 6.15.

*4.2.5. 1-(2-Nitrophenylsulfonyl)-2-(phenylthiomethyl)pyrrolidine (**3f**) (Table 1, entry 6).* White solid; mp 78–80 °C; IR (film) 1539, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J*=8.4 Hz, 1H), 7.70–7.63 (m, 1H), 7.63–7.54 (m, 2H), 7.44–7.37 (m, 2H), 7.36–7.28 (m, 2H), 7.22 (t, *J*=7.2 Hz, 1H), 4.09–4.00 (m, 1H), 3.59–3.40 (m, 3H), 2.83 (dd, *J*=13.6, 10.4 Hz, 1H), 2.09–1.88 (m, 3H), 1.88–1.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 135.4, 133.8, 131.8, 131.6, 130.9, 129.4, 129.2, 126.4, 124.1, 59.8, 49.4, 38.3, 30.6, 24.1; Anal. Calcd for $C_{17}H_{18}N_2O_4S_2$: C, 53.95; H, 4.79; N, 7.40; found: C, 53.99; H, 4.79; N, 7.32.

*4.2.6. threo-1-(2-Nitrophenylsulfonyl)-2-[1-(phenylthio)ethyl]-pyrrolidine (**3g**) (Table 1, entry 7).* Light yellow solid; mp 121–122 °C; IR (film) 1545, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.46 (m, 6H), 7.40–7.33 (m, 2H), 7.33–7.26 (m, 1H), 4.03–3.93 (m, 2H), 3.65–3.55 (m, 1H), 3.52–3.40 (m, 1H), 2.10–1.80 (m, 3H), 1.73–1.61 (m, 1H), 1.28 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 134.8, 133.7, 131.9, 131.4, 131.2, 129.3, 127.2, 124.1, 62.6, 50.7, 45.9, 26.6, 25.1, 13.9; Anal. Calcd for $C_{18}H_{20}N_2O_4S_2$: C, 55.08; H, 5.14; N, 7.14; found: C, 54.96; H, 5.14; N, 7.11.

*4.2.7. threo-2-[2,2-Dimethyl-1-(phenylthio)propyl]-1-(2-nitro-phenylsulfonyl)pyrrolidine (**3h**) (Table 1, entry 8).* White solid; mp 177–178 °C; IR (film) 1544, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J*=7.6 Hz, 1H), 7.64 (t, *J*=7.6 Hz, 1H), 7.60–7.50 (m, 4H), 7.30 (t, *J*=7.6 Hz, 2H), 7.22 (t, *J*=7.2 Hz, 1H), 4.42–4.35 (m, 1H), 3.27–3.17 (m, 1H), 3.15–3.01 (m, 2H), 2.04–1.91 (m, 1H), 1.85–1.75 (m, 1H), 1.61–1.42 (m, 2H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 137.9, 133.4, 132.2, 132.0, 131.7, 131.2, 129.0, 126.8, 124.1, 68.1, 62.9, 49.1, 36.1, 33.4, 29.2, 24.1; HRMS (EI) Calcd for $C_{21}H_{26}N_2O_4S_2$ (M^+): 434.1334; found: 434.1339.

*4.2.8. erythro-1-(2-Nitrophenylsulfonyl)-2-[1-(phenylthio)-hexyl] pyrrolidine (**3i**) (Table 1, entry 9).* Yellow oil; IR (film) 1545, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J*=7.6 Hz, 1H), 7.63 (t, *J*=7.6 Hz, 1H), 7.55 (t, *J*=8.4 Hz, 2H), 7.40 (d, *J*=7.6 Hz, 2H), 7.24 (t, *J*=7.6 Hz, 2H), 7.18 (t, *J*=7.6 Hz, 1H), 4.34–4.21 (m, 1H), 3.70–3.57 (m, 2H), 3.49–3.38 (m, 1H), 2.10–1.90 (m, 3H), 1.72–1.37 (m, 5H), 1.37–1.19 (m, 4H), 0.87 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 135.9, 133.6, 132.5, 131.6, 131.4, 130.9, 129.1, 126.8, 124.1, 63.7, 55.4, 50.3, 34.4, 31.8, 28.1, 27.2, 25.5, 22.7, 14.2; Anal. Calcd for $C_{22}H_{28}N_2O_4S_2$: C, 58.90; H, 6.29; N, 6.24; found: C, 58.62; H, 6.35; N, 6.04.

*4.2.9. erythro-2-[(Cyclohexyl)(phenylthio)methyl]-1-(2-nitro-phenylsulfonyl)pyrrolidine (**3j**) (Table 1, entry 10).* White solid; mp 144–145 °C; IR (film) 1545, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J*=8.0 Hz, 1H), 7.66–7.59 (m, 1H), 7.58–7.51 (m, 2H), 7.41 (d, *J*=7.6 Hz, 2H), 7.25–7.18 (m, 2H), 7.14 (t, *J*=7.2 Hz, 1H), 4.50–4.43 (m, 1H), 3.66–3.58 (m, 1H), 3.58–3.52 (m, 1H), 3.50–3.41 (m, 1H), 2.14–2.05 (m, 1H), 2.04–1.91 (m, 3H), 1.89–1.69 (m, 3H), 1.68–1.49 (m, 3H), 1.39–1.07 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 137.5, 133.5, 132.6, 131.5, 130.9, 130.7, 129.1, 126.4, 124.2, 62.4, 62.3, 50.0, 42.5, 31.4, 31.1, 28.9, 26.6, 26.53, 26.49, 25.7; Anal. Calcd for $C_{23}H_{28}N_2O_4S_2$: C, 59.97; H, 6.13; N, 6.08; found: C, 59.99; H, 6.18; N, 6.14.

*4.2.10. erythro-2-[3-Methyl-1-(phenylthio)butyl]-1-(2-nitro-phenylsulfonyl)pyrrolidine (**3k**) (Table 1, entry 11).* White solid; mp 79–80 °C; IR (film) 1545, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J*=8.0 Hz, 1H), 7.66–7.59 (m, 1H), 7.59–7.52 (m, 2H), 7.40 (d, *J*=7.6 Hz, 2H), 7.29–7.21 (m, 2H), 7.20–7.15 (m, 1H), 4.30–4.20 (m, 1H), 3.81–3.72 (m, 1H), 3.67–3.58 (m, 1H), 3.48–3.38 (m, 1H), 2.10–1.86 (m, 4H), 1.69–1.56 (m, 1H), 1.51–1.39 (m, 2H), 0.93 (d, *J*=6.8 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 135.8, 133.5, 132.6, 131.6, 131.4, 130.9, 129.1, 126.8, 124.2, 63.8, 53.2, 50.3, 43.7, 28.0, 25.7, 25.5, 22.8, 22.6; Anal. Calcd for $C_{21}H_{26}N_2O_4S_2$: C, 58.04; H, 6.03; N, 6.45; found: C, 58.07; H, 6.08; N, 6.47.

*4.2.11. erythro-2-Methyl-1-(2-nitrophenylsulfonyl)-2-[1-(phenylthio)hexyl]pyrrolidine (**3l**) (Table 1, entry 12).* Yellow oil; IR (film) 1545, 1373, 1161 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J*=8.0 Hz, 1H), 7.58–7.38 (m, 5H), 7.28–7.21 (m, 2H), 7.15 (t, *J*=7.2 Hz, 1H), 4.12 (dd, *J*=8.8, 3.2 Hz, 1H), 3.72–3.63 (m, 1H), 3.42–3.32 (m, 1H), 2.36–2.26 (m, 1H), 1.97–1.73 (m, 4H), 1.65 (s, 3H), 1.65–1.42 (m, 2H), 1.41–1.28 (m, 1H), 1.28–1.10 (m, 4H), 0.80 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 136.6, 134.2, 133.3, 131.5, 130.8, 130.1, 129.0, 126.4, 123.8, 73.5, 58.8, 50.9, 37.6, 34.2, 31.9, 27.6, 25.8, 23.3, 22.5, 14.1; HRMS (EI) Calcd for $C_{23}H_{30}N_2O_4S_2$ (M^+): 462.1647; found: 462.1652.

4.3. Representative procedure for rearrangement of pyrrolidine to piperidine (Table 2, entry 2)

To a stirred solution of **3c** (0.223 g, 0.50 mmol) in CH_2Cl_2 (2.5 mL) was added TfOH (0.015 g, 0.10 mmol) at 25 °C. Upon stirring at 25 °C for 48 h, the reaction mixture was filtered through a plug of silica gel with CH_2Cl_2 (50 mL) as eluent, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=100:1) to give compound **4c** as pale yellow oil (0.178 g, 80%).

*4.3.1. syn-2-Pentyl-3-phenylthio-1-tosylpiperidine (**4b**) (Table 2, entry 1).* Yellow oil; IR (film) 1466, 1334, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J*=8.0 Hz, 2H), 7.34–7.26 (m, 5H), 7.23 (d, *J*=8.0 Hz, 2H), 4.00–3.93 (m, 1H), 3.90–3.82 (m, 1H), 3.12 (dt, *J*=12.8, 4.0 Hz, 1H), 3.04–2.92 (m, 1H), 2.41 (s, 3H), 1.85–1.00 (m, 12H), 0.83 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.9, 134.3, 131.8, 129.8, 129.2, 127.3, 127.1, 56.1, 47.9, 39.5, 31.6, 25.9, 25.8, 25.7, 24.0, 22.6, 21.6, 14.1; HRMS (EI) Calcd for $C_{23}H_{31}NO_2S_2$ (M^+): 417.1796; found: 417.1801.

*4.3.2. syn-1-(Mesitylsulfonyl)-2-pentyl-3-(phenylthio)piperidine (**4c**) (Table 2, entry 2).* White solid; mp 73–75 °C; IR (film) 1604,

1439, 1322, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 7.33–7.19 (m, 3H), 6.85 (s, 2H), 4.07–3.98 (m, 1H), 3.94–3.87 (m, 1H), 3.48–3.39 (m, 1H), 3.02–2.92 (m, 1H), 2.45 (s, 6H), 2.25 (s, 3H), 2.01–1.92 (m, 1H), 1.85–1.49 (m, 5H), 1.09–0.76 (m, 5H), 0.68 (t, J=7.2 Hz, 3H), 0.45–0.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 140.0, 134.4, 133.9, 132.0, 131.5, 129.3, 127.1, 55.9, 47.8, 39.4, 31.5, 27.4, 26.3, 25.5, 24.5, 23.0, 22.7, 21.0, 13.9; Anal. Calcd for $C_{25}H_{35}NO_2S_2$: C, 67.37; H, 7.92; N, 3.14; found: C, 67.60; H, 7.99; N, 3.09.

*4.3.3. syn-1-(4-Nitrophenylsulfonyl)-2-pentyl-3-(phenylthio)-piperidine (**4d**) (Table 2, entry 3).* White solid; IR (film) 1530, 1349, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J=8.8 Hz, 2H), 7.86 (d, J=8.8 Hz, 2H), 7.38–7.30 (m, 5H), 4.02–3.93 (m, 1H), 3.93–3.82 (m, 1H), 3.11–2.94 (m, 2H), 1.90–1.57 (m, 5H), 1.47–1.10 (m, 6H), 1.09–0.97 (m, 1H), 0.83 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 147.5, 134.0, 132.3, 129.3, 128.1, 127.9, 124.5, 56.8, 48.9, 39.8, 31.5, 25.9, 25.8, 25.7, 23.9, 22.6, 14.1; HRMS (EI) Calcd for $C_{22}H_{28}N_2O_4S_2$ (M^+): 448.1491; found: 448.1496.

*4.3.4. syn-1-(2-Nitrophenylsulfonyl)-2-pentyl-3-(phenylthio)-piperidine (**4e**) (Table 2, entry 4).* Yellow oil; IR (film) 1544, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92–7.86 (m, 1H), 7.68–7.54 (m, 3H), 7.47–7.41 (m, 2H), 7.38–7.31 (m, 2H), 7.30–7.23 (m, 1H), 4.00–3.86 (m, 2H), 3.59–3.50 (m, 1H), 3.12–3.01 (m, 1H), 1.95–1.86 (m, 1H), 1.81–1.58 (m, 5H), 1.14–0.99 (m, 5H), 0.78–0.63 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 134.5, 134.3, 133.5, 131.8, 131.5, 131.1, 129.3, 127.3, 124.4, 57.2, 48.5, 40.1, 31.6, 26.9, 25.9, 25.6, 24.3, 22.6, 14.0; Anal. Calcd for $C_{22}H_{28}N_2O_4S_2$: C, 58.90; H, 6.29; N, 6.24; found: C, 58.66; H, 6.25; N, 5.93.

*4.3.5. 1-(2-Nitrophenylsulfonyl)-3-(phenylthio)piperidine (**4f**) (Table 2, entry 5).* Yellow oil; IR (film) 1545, 1166 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91–7.85 (m, 1H), 7.71–7.53 (m, 3H), 7.43–7.37 (m, 2H), 7.34–7.19 (m, 3H), 3.95–3.84 (m, 1H), 3.77–3.68 (m, 1H), 3.26–3.15 (m, 1H), 2.88–2.74 (m, 2H), 2.15–2.06 (m, 1H), 1.90–1.78 (m, 1H), 1.76–1.62 (m, 1H), 1.46–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 133.8, 133.2, 132.1, 132.0, 131.8, 130.9, 129.3, 127.6, 124.3, 51.4, 46.1, 43.7, 30.4, 25.4; HRMS (ESI) Calcd for $C_{17}H_{19}N_2O_4S_2$ (M+H): 379.0781; found: 379.0779.

*4.3.6. syn-2-Methyl-1-(2-nitrophenylsulfonyl)-3-(phenylthio)-piperidine (**4g**) (Table 2, entry 6).* Yellow oil; IR (film) 1544, 1169 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J=8.0 Hz, 1H), 7.70–7.57 (m, 3H), 7.41–7.35 (m, 2H), 7.34–7.21 (m, 3H), 4.23–4.13 (m, 1H), 3.75–3.66 (m, 1H), 3.48–3.37 (m, 1H), 3.16–3.05 (m, 1H), 1.92–1.85 (m, 1H), 1.79–1.61 (m, 3H), 1.25 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 134.0, 133.8, 133.6, 131.9, 131.3, 131.0, 129.3, 127.3, 124.5, 52.0, 48.1, 39.9, 26.3, 24.9, 11.03; HRMS (ESI) Calcd for $C_{18}H_{21}N_2O_4S_2$ (M+H): 393.0937; found: 393.0939.

*4.3.7. anti-1-(2-Nitrophenylsulfonyl)-2-pentyl-3-(phenylthio)-piperidine (**4i**) (Table 2, entry 8).* Pale yellow oil; IR (film) 1541, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J=8.0 Hz, 1H), 7.69–7.55 (m, 3H), 7.30–7.18 (m, 5H), 4.06–3.97 (m, 1H), 3.97–3.89 (m, 1H), 3.46–3.38 (m, 1H), 3.19–3.08 (m, 1H), 2.19–1.91 (m, 2H), 1.87–1.60 (m, 3H), 1.58–1.48 (m, 1H), 1.33–1.12 (m, 6H), 0.85 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 135.3, 134.6, 133.3, 131.7, 131.4, 131.3, 129.2, 127.1, 124.2, 58.1, 46.3, 41.3, 31.5, 31.1, 26.3, 23.5, 22.5, 20.3, 14.1; HRMS (EI) Calcd for $C_{22}H_{28}N_2O_4S_2$ (M^+): 448.1490; found: 448.1496.

*4.3.8. anti-2-Cyclohexyl-1-(2-nitrophenylsulfonyl)-3-(phenylthio)piperidine (**4j**) (Table 2, entry 9).* White solid; mp 137–138 °C; IR (film) 1544, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20–8.16 (m, 1H), 7.66–7.53 (m, 3H), 7.31–7.18 (m, 5H), 4.03–3.94 (m, 1H), 3.90–3.82 (m, 1H), 3.65–3.57 (m, 1H), 3.05–2.94 (m, 1H), 2.05–1.89 (m, 2H), 1.84–1.69 (m, 6H), 1.69–1.60 (m, 1H), 1.51–1.41 (m, 1H), 1.31–0.96 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 135.6, 135.1, 133.1, 132.0, 131.2, 131.1, 129.3, 127.1, 123.7, 63.9, 45.2, 42.0, 37.7, 31.5, 29.8, 26.6, 26.5, 26.2, 24.2, 20.2; Anal. Calcd for $C_{23}H_{28}N_2O_4S_2$: C, 59.97; H, 6.13; N, 6.08; found: C, 60.38; H, 6.28; N, 6.03.

*4.3.9. anti-2-(2-Methylpropyl)-1-(2-nitrophenylsulfonyl)-3-(phenylthio)piperidine (**4k**) (Table 2, entry 10).* Yellow oil; IR (film) 1537, 1469, 1169 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J=7.2 Hz, 1H), 7.68–7.58 (m, 3H), 7.30–7.18 (m, 5H), 4.11–4.04 (m, 1H), 3.94–3.86 (m, 1H), 3.40–3.34 (m, 1H), 3.18–3.09 (m, 1H), 2.15–1.91 (m, 2H), 1.85–1.71 (m, 2H), 1.60–1.42 (m, 3H), 0.88 (d, J=6.4 Hz, 3H), 0.79 (d, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 135.2, 134.5, 133.3, 132.1, 131.7, 131.4, 129.2, 127.4, 124.3, 56.3, 47.0, 41.3, 40.0, 25.5, 23.6, 21.6, 20.3; HRMS (EI) Calcd for $C_{21}H_{26}N_2O_4S_2$ (M^+): 434.1334; found: 434.1340.

4.4. Procedure for Scheme 3

*4.4.1. erythro-1-(Mesitylsulfonyl)-2-[1-(hydroxy)hexyl]pyrrolidine (**6**).* γ-Amino–alkene **1m** (3.20 g, 9.49 mmol) was subjected to the asymmetric epoxidation conditions[14] to give the crude epoxide, which was dissolved in CH_2Cl_2 (50 mL), followed by the addition of CSA (0.221 g, 0.95 mmol). Upon stirring at 25 °C for 1.5 h, the reaction mixture was filtered through a plug of silica gel with CH_2Cl_2 as eluent, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=30:1 to 20:1 to 5:1) to afford compound **6** as yellow oil (2.04 g, 61% over two steps). $[\alpha]_D^{20}=-108.5$ (c 0.97, $CHCl_3$); IR (film) 3257, 1457, 1309, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, 2H), 3.85–3.78 (m, 1H), 3.77–3.68 (m, 1H), 3.46–3.37 (m, 1H), 3.14–2.96 (m, 1H), 2.64 (s, 6H), 2.29 (s, 3H), 2.06–1.72 (m, 5H), 1.46–1.13 (m, 8H), 0.87 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 140.2, 133.1, 132.3, 72.3, 64.0, 49.3, 33.3, 31.9, 25.9, 25.7, 25.4, 23.0, 22.7, 21.1, 14.2; HRMS (EI) Calcd for $C_{19}H_{31}NO_3S$ (M^+): 353.2025; found: 353.2030.

*4.4.2. threo-1-(Mesitylsulfonyl)-2-[1-(phenylthio)hexyl]pyrrolidine (**3m**).* To a solution of alcohol **6** (1.73 g, 4.90 mmol) and Et_3N (1.49 g, 14.70 mmol) in dry THF (30 mL) was added MsCl (0.842 g, 7.35 mmol) dropwise at 0 °C.[15] Upon stirring at 25 °C for 3 h, the reaction mixture was filtered through a plug of silica gel with ethyl acetate as eluent and concentrated to give mesylate **7**, which was dissolved in dry THF (50 mL), followed by the addition of PhSNa[16] (1.29 g, 9.80 mmol). The reaction mixture was refluxed for 24 h, cooled to rt, diluted with H_2O and ethyl acetate, extracted with ethyl acetate (3×70 mL), washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=50:1) to give a mixture of **3m** and **8** (1:0.6) as yellow oil (0.834 g, 27% for **3m** from **6**) (88% ee for **3m**).

4.5. Procedure for Scheme 4

*4.5.1. 6-(tert-Butyldiphenylsilyloxy)hex-1-en-3-ol (**10**).* To a solution of aldehyde **9**[17] (6.57 g, 20.14 mmol) in dry THF (25 mL) was added dropwise a solution of vinylmagnesium bromide in THF (1.0 M) (30.2 mL, 30.2 mmol) at −40 °C under N_2.[18] Upon warming to rt and stirring for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ethyl ether (3×80 mL), washed with brine and dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=10:1 to 5:1) to afford allylic alcohol **10** as colourless oil (6.37 g, 89%). IR (film) 3384, 1428, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71–7.64 (m, 4H), 7.47–7.36 (m, 6H), 5.93–5.82 (m, 1H), 5.23 (dt, J=17.2, 1.6 Hz, 1H), 5.11 (dt, J=10.4, 1.2 Hz, 1H), 4.19–4.10

(m, 1H), 3.74–3.66 (m, 2H), 2.09 (d, *J*=4.4 Hz, 1H), 1.73–1.60 (m, 4H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 135.8, 134.0, 129.8, 127.9, 114.7, 73.0, 64.2, 34.1, 28.6, 27.1, 19.4; HRMS (ESI) Calcd for $C_{22}H_{30}NaO_2Si$ (M+Na): 377.1907; found: 377.1909.

*4.5.2. (E)-Ethyl 8-(tert-butyldiphenylsilyloxy)oct-4-enoate (**11**).* A stirred mixture of propionic acid (0.133 g, 1.8 mmol), triethyl orthoacetate (17.52 g, 108.0 mmol), and allylic alcohol **10** (6.37 g, 18.0 mmol) was heated in an oil bath (138 °C).[18–20] Ethanol, formed during the reaction, was simultaneously removed by distillation. Upon heating for 4 h, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $NaHCO_3$, and diluted with CH_2Cl_2. Upon addition of an aqueous HCl-solution (1 M) (100 mL), the reaction mixture was stirred for 30 min, extracted with CH_2Cl_2 (3×100 mL), washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=50:1) to afford ester **11** as colourless oil (6.29 g, 82%). IR (film) 1737, 1428, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.66 (m, 4H), 7.46–7.36 (m, 6H), 5.53–5.37 (m, 2H), 4.14 (q, *J*=7.2 Hz, 2H), 3.68 (t, *J*=6.4 Hz, 2H), 2.39–2.26 (m, 4H), 2.10 (q, *J*=6.4 Hz, 2H), 1.64 (quintet, *J*=6.8 Hz, 2H), 1.27 (t, *J*=6.8 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 135.8, 134.3, 131.3, 129.7, 128.6, 127.8, 63.4, 60.4, 34.6, 32.5, 28.9, 28.1, 27.1, 19.4, 14.5; HRMS (ESI) Calcd for $C_{26}H_{36}NaO_3Si$ (M+Na): 447.2326; found: 447.2331.

*4.5.3. (E)-N-[8-(tert-Butyldiphenylsilyloxy)oct-4-enyl]mesityl-sulfonamide (**13**).* To a suspension of $LiAlH_4$ (1.08 g, 28.27 mmol) in dry Et_2O (50 mL) was added dropwise a solution of ester **11** (12.08 g, 28.47 mmol) in Et_2O (50 mL) at 0 °C. Upon stirring at rt for 2 h, the reaction mixture was cooled to 0 °C, quenched by slow addition of H_2O until no bubble was seen, filtered through a plug of silica gel with Et_2O as eluent, and concentrated to afford crude alcohol **12** as colourless oil (10.0 g, 92%).

Alcohol **12** (13.12 g, 34.30 mmol) was dissolved in THF (100 mL), followed by the successive addition of MsCl (4.72 g, 41.20 mmol) and Et_3N (17.30 g, 171.0 mmol) at 0 °C. Upon stirring at rt for 1.5 h, the reaction mixture was filtered through a plug of silica gel with ethyl acetate as eluent and concentrated to give the mesylate as yellow oil.

A mixture of KOH (2.88 g, 51.45 mmol) and 2,4,6-trimethylbenzenesulfonylamide (10.24 g, 51.45 mmol) in DMF (200 mL) was stirred at 120 °C for 30 min. To this hot solution was dropwise added, a solution of the above mesylate in DMF (20 mL). The resulting reaction mixture was stirred at 120 °C for 5 h and cooled to rt, diluted with H_2O, extracted with Et_2O for three times, washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate/dichloromethane=100:1:1 to 50:1:1 to 30:1:1) to afford compound **13** as pale yellow oil (12.88 g, 67% over two steps). IR (film) 3300, 1323, 1154, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.61 (m, 4H), 7.46–7.32 (m, 6H), 6.95 (s, 2H), 5.36–5.18 (m, 2H), 4.39 (t, *J*=6.0 Hz, 1H), 3.63 (t, *J*=6.4 Hz, 2H), 2.87 (q, *J*=6.8 Hz, 2H), 2.63 (s, 6H), 2.29 (s, 3H), 2.06–1.98 (m, 2H), 1.97–1.88 (m, 2H), 1.62–1.52 (m, 2H), 1.52–1.42 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 139.3, 135.8, 134.3, 133.9, 132.1, 131.5, 129.7, 129.0, 127.8, 63.4, 42.2, 32.5, 29.7, 29.5, 28.9, 27.1, 23.2, 21.1, 19.4; HRMS (ESI) Calcd for $C_{33}H_{45}NNaO_3SSi$ (M+Na): 586.2782; found: 586.2796.

*4.5.4. threo-1-(Mesitylsulfonyl)-2-[(4-mesitylsulfonylamino-1-phenylthio)butyl]pyrrolidine (**16**).* Compound **13** was converted to compound **14** in a manner similar to the reaction sequence from **1m** to **3m**. A mixture of **14** and **15** was obtained (2.58 g, **14**:**15**=2:1, 35% yield for **14** from **13**). Compound **14** was deprotected with TBAF and subsequently converted to compound **16** (1.07 g, 64% over three steps) in a manner similar to the reaction sequence from **12** to **13**. Compound **16**: white solid; mp 45–47 °C; $[\alpha]_D^{20}$=−3.8 (*c* 0.89, $CHCl_3$) (88% ee); IR (film) 3315, 1603, 1314, 1150 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.14 (m, 5H), 6.95 (s, 2H), 6.88 (s, 2H), 4.75–4.65 (m, 1H), 4.16–4.08 (m, 1H), 3.48–3.39 (m, 1H), 3.23–3.12 (m, 1H), 3.09–3.00 (m, 1H), 2.96–2.79 (m, 2H), 2.65 (s, 6H), 2.47 (s, 6H), 2.30 (s, 3H), 2.29 (s, 3H), 2.17–2.03 (m, 1H), 1.99–1.89 (m, 1H), 1.86–1.65 (m, 4H), 1.34–1.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 142.3, 140.3, 139.2, 135.0, 134.1, 133.1, 132.3, 132.2, 131.2, 129.3, 127.1, 62.3, 51.7, 49.7, 42.2, 28.1, 27.7, 25.6, 25.2, 23.2, 23.0, 22.9, 21.2, 21.1; HRMS (EI) Calcd for $C_{32}H_{42}N_2O_4S_3$ (M^+): 614.2307; found: 614.2314.

4.6. Procedure for Scheme 5

To a stirred solution of **3m** (mixture of **3m** and **8**: 0.192 g, **3m**:**8**=1:0.6, 0.30 mmol for **3m**) in CH_2Cl_2 (3 mL) was added TfOH (0.045 g, 0.30 mmol) at 25 °C. Upon stirring at 25 °C for 24 h, the reaction mixture was filtered through a plug of silica gel with CH_2Cl_2 (50 mL) as eluent, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate=100:1) to give compound **4m** as pale yellow oil (0.105 g, 78%). $[\alpha]_D^{20}$=+148 (*c* 0.80, $CHCl_3$) (88% ee).

4.7. Procedure for Scheme 6

A solution of **16** (0.123 g, 0.20 mmol) and TfOH (0.030 g, 0.20 mmol) in CH_2Cl_2 (2 mL) was stirred at 27 °C for 24 h. The reaction mixture was filtered through a plug of silica gel with ethyl acetate as eluent, concentrated, and purified by column chromatography (silica gel, eluent: petroleum ether/dichloromethane/ethyl acetate=20:2:1) to give a mixture of **16** and **19** (ratio **16**:**19**=16:84) as white solid (0.109 g, 74% for **19** from **16**).

syn-1-(Mesitylsulfonyl)-2-[(3-mesitylsulfonylamino)propyl]-3-(phenylthio)piperidine (**19**) White solid; IR (film) 3311, 1320, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.35 (m, 2H), 7.31–7.20 (m, 3H), 6.94 (s, 2H), 6.86 (s, 2H), 4.15–4.07 (m, 1H), 3.90–3.82 (m, 1H), 3.80–3.72 (m, 1H), 3.50–3.41 (m, 1H), 2.92–2.79 (m, 1H), 2.59 (s, 6H), 2.58–2.50 (m, 2H), 2.42 (s, 6H), 2.30 (s, 3H), 2.26 (s, 3H), 1.99–1.88 (m, 1H), 1.84–1.49 (m, 5H), 1.21–1.16 (m, 1H), 0.74–0.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 142.3, 139.9, 139.2, 134.1, 134.0, 133.7, 132.2, 131.3, 129.4, 127.3, 55.3, 47.7, 42.1, 39.4, 27.0, 26.1, 26.0, 23.1, 23.0, 21.6, 21.13, 21.10; HRMS (ESI) Calcd for $C_{32}H_{43}N_2O_4S_3$ (M+H): 615.2380; found: 615.2390.

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Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.08.043.

References and notes

1. For a leading reference, see: O'Hagan, D. *Nat. Prod. Rep.* **2000**, *17*, 435.
2. For leading references on intramolecular halo–amination of olefins, see: (a) Jones, A. D.; Knight, D. W.; Hibbs, D. E. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1182; (b) Minakata, S.; Morino, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2006**, *8*, 3335; (c) Majumdar, K. C.; Ray, K.; Ponra, S. *Tetrahedron Lett.* **2010**, *51*, 5437; (d) Moriyama, K.; Izumisawa, Y.; Togo, H. *J. Org. Chem.* **2011**, *76*, 7249.

3. For a leading review on intramolecular selenoamination of γ-amino−alkenes with PhSeX or PhSeSePh, see: Petragnani, N.; Stefani, H. A.; Valduga, C. J. *Tetrahedron* **2001**, *57*, 1411.
4. For leading references on intramolecular selenoamination of γ-amino−alkenes with PhSeX, see: (a) Clive, D. L. J.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1978**, 379; (b) Outurquin, F.; Pannecoucke, X.; Berthe, B.; Paulmier, C. *Eur. J. Org. Chem.* **2002**, 1007; (c) Jones, A. D.; Redfern, A. L.; Knight, D. W.; Morgan, I. R.; Williams, A. C. *Tetrahedron* **2006**, *62*, 9247; (d) Lim, H. J.; RajanBabu, T. V. *Org. Lett.* **2009**, *11*, 2924.
5. For leading references on intramolecular sulfamination of γ-amino−alkenes with ArSX, see: (a) Ohsawa, T.; Ihara, M.; Fukumoto, K.; Kametani, T. *J. Org. Chem.* **1983**, *48*, 3644; (b) Vas'kevich, A. I.; Tsizorik, N. M.; Rusanov, E. B.; Stanitets, V. I.; Vovk, M. V. *Russ. J. Org. Chem.* **2011**, *47*, 1146.
6. For a leading review on electrophilic sulfur additions to olefins, see: Rayner, C. M. In *Organosulfur Chemistry: Synthetic Aspects*; Bullman-Page, P., Ed.; Academic: London, 1995; p 89.
7. For leading references on acid-promoted addition of RS or RSe to olefins with RS−N or RSe−N reagents, see: (a) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704; (b) Caserio, M. C.; Kim, J. K. *J. Am. Chem. Soc.* **1982**, *104*, 3231; (c) Brownbridge, P. *Tetrahedron Lett.* **1984**, *25*, 3759; (d) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *Tetrahedron* **1986**, *42*, 1145; (e) Brownbridge, P. *J. Chem. Soc., Chem. Commun.* **1987**, 1280; (f) Tiecco, M.; Testaferri, L.; Bagnoli, L.; Scarponi, C. *Tetrahedron: Asymmetry* **2008**, *19*, 2411.
8. For leading references on acid-promoted addition of RS to olefins with RSSR or RSOR reagents, see: (a) Trost, B. M.; Ochiai, M.; McDougal, P. G. *J. Am. Chem. Soc.* **1978**, *100*, 7103; (b) Edstrom, E. D.; Livinghouse, T. *J. Am. Chem. Soc.* **1986**, *108*, 1334; (c) Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1987**, *28*, 2723; (d) Taniguchi, N. *J. Org. Chem.* **2006**, *71*, 7874; (e) Yamagiwa, N.; Suto, Y.; Torisawa, Y. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6197.
9. Wang, H.; Huang, D.; Cheng, D.; Li, L.; Shi, Y. *Org. Lett.* **2011**, *13*, 1650.
10. (a) Chang, L. L.; Denney, D. B.; Denney, D. Z.; Kazior, R. J. *J. Am. Chem. Soc.* **1977**, *99*, 2293; (b) Guan, H.; Wang, H.; Huang, D.; Shi, Y. *Tetrahedron* **2012**, *68*, 2728.
11. When substrate **1d** was treated with *N*-propylthiosuccinimide (1.2 equiv) and CSA (0.1 equiv) in CH_2Cl_2 at 25 °C for 24 h, only 13% conversion was obtained
12. For an example of rearrangement of piperidine to pyrrolidine under acidic conditions, see: Fox, D. J.; Morley, T. J.; Taylor, S.; Warren, S. *Org. Biomol. Chem.* **2005**, *3*, 1369.
13. For leading references on tetrahydrofuran rearrangement to tetrahydropyran via thiiranium and seleniranium ions, see: (a) Gruttadauria, M.; Lo Meo, P.; Noto, R. *Tetrahedron* **2001**, *57*, 1819; (b) Gruttadauria, M.; Noto, R. *J. Heterocycl. Chem.* **2001**, *38*, 765; (c) Fox, D. J.; House, D.; Warren, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2462; (d) Gruttadauria, M.; Aprile, C.; Noto, R. *Tetrahedron Lett.* **2002**, *43*, 1669; (e) Aprile, C.; Gruttadauria, M.; Amato, M. E.; D'Anna, F.; Lo Meo, P.; Riela, S.; Noto, R. *Tetrahedron* **2003**, *59*, 2241.
14. (a) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224; (b) Wang, Z. X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 3099.
15. Marcotullio, M. C.; Campagna, V.; Sternativo, S.; Costantino, F.; Curini, M. *Synthesis* **2006**, *16*, 2760.
16. Kuniyasu, H.; Yamashita, F.; Hirai, T.; Ye, J.; Fujiwara, S.; Kambe, N. *Organometallics* **2006**, *25*, 566.
17. Keum, G.; Hwang, C. H.; Kang, S. B.; Kim, Y.; Lee, E. *J. Am. Chem. Soc.* **2005**, *127*, 10396.
18. Grünanger, C. U.; Breit, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 967.
19. Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.-T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
20. Johnson, W. S.; Gravestock, M. B.; McCarry, B. E. *J. Am. Chem. Soc.* **1971**, *93*, 4332.
21. For leading references on enantiomerically enriched thiiranium ions, see: (a) Branchaud, B. P.; Blanchette, H. S. *Tetrahedron Lett.* **2002**, *43*, 351; (b) Denmark, S. E.; Vogler, T. *Chem.—Eur. J.* **2009**, *15*, 11737; (c) Denmark, S. E.; Kornfilt, D. J. P.; Vogler, J. *J. Am. Chem. Soc.* **2011**, *133*, 15308.
22. For a leading reference on studies of stability of thiiranium ions, see: Denmark, S. E.; Collins, W. R.; Cullen, M. D. *J. Am. Chem. Soc.* **2009**, *131*, 3490.
23. For a leading review on pyrrolidine rearrangement to piperidine via aziridinium ions, see: Métro, T. X.; Pardo, D. G.; Cossy, J. *Chem.—Eur. J.* **2009**, *15*, 1064.
24. Ryu, J. S.; Marks, T. J.; McDonald, F. E. *Org. Lett.* **2001**, *3*, 3091.
25. Jung, H. H.; Floreancig, P. E. *J. Org. Chem.* **2007**, *72*, 7359.
26. Kang, S. H.; Lee, S. B.; Park, C. M. *J. Am. Chem. Soc.* **2003**, *125*, 15748.